ENTERED



OIPE

RAW SEQUENCE LISTING DATE: 01/02/2002 PATENT APPLICATION: US/10/017,736 TIME: 11:32:09

Input Set : A:\seqlist.txt

Output Set: N:\CRF3\01022002\J017736.raw

4 <110> APPLICANT: Boehringer Ingelheim (Canada) Ltd. 6 <120> TITLE OF INVENTION: Purified Active HCV NS2/3 Protease 9 <130> FILE REFERENCE: 13/082

C--> 11 <140> CURRENT APPLICATION NUMBER: US/10/017,736

C--> 11 <141> CURRENT FILING DATE: 2001-12-14 11 <150> PRIOR APPLICATION NUMBER: 60/256,031

12 <151> PRIOR FILING DATE: 2000-12-15 14 <160> NUMBER OF SEQ ID NOS: 21

16 <170> SOFTWARE: FastSEQ for Windows Version 4.0

18 <210> SEQ ID NO: 1 19 <211> LENGTH: 1230 20 <212> TYPE: DNA

21 <213> ORGANISM: HCV

23 <220> FEATURE:

24 <221> NAME/KEY: CDS

25 <222> LOCATION: (1)...(1230) 27 <400> SEQUENCE: 1 28 atg gac cgg gag atg gct gca tcg tgc gga ggc gcg gtt ttc ata ggt 29 Met Asp Arg Glu Met Ala Ala Ser Cys Gly Gly Ala Val Phe Ile Gly 5 32 ctt gca ctc ttg acc ttg tca.cca tac tat aaa gtg ctc ctc gct agg 96 33 Leu Ala Leu Leu Thr Leu Ser Pro Tyr Tyr Lys Val Leu Leu Ala Arg 2.5 36 ctc ata tgg tgg tta cag tat tta atc acc aga gtc gag gcg cac ttg 144 37 Leu Ile Trp Trp Leu Gln Tyr Leu Ile Thr Arg Val Glu Ala His Leu 38 35 40 caa gtg tgg atc ccc cct ctc aat gtt cgg gga ggc cgc gat gcc atc 41 Gln Val Trp Ile Pro Pro Leu Asn Val Arg Gly Gly Arg Asp Ala Ile 55 44 atc ctc ctc acg tgc gca gtc cac cca gag cta atc ttt gac atc acc 45 Ile Leu Leu Thr Cys Ala Val His Pro Glu Leu Ile Phe Asp Ile Thr 75 48 aaa ctc ctg ctc gcc ata ttc ggt ccg ctc atg gtg ctc cag gca ggc 288 49 Lys Leu Leu Leu Ala Ile Phe Gly Pro Leu Met Val Leu Gln Ala Gly 85 52 ata acc aaa gtg ccg tac ttc gtg cgt gcg cag ggg ctc att cgt gcg 53 Ile Thr Lys Val Pro Tyr Phe Val Arg Ala Gln Gly Leu Ile Arg Ala 56 tgt atg ttg gtg cgg aag gct gcg ggg ggt cat tat gtc caa atg gcc 384 57 Cys Met Leu Val Arg Lys Ala Ala Gly Gly His Tyr Val Gln Met Ala 120 60 ttc atg aag cta gct gcg ctg aca ggt acg tac gtt tat gac cat ctc 61 Phe Met Lys Leu Ala Ala Leu Thr Gly Thr Tyr Val Tyr Asp His Leu 135 64 act cca ttg cag gat tgg gcc cac gcg ggc cta cga gac ctt gca gtg 480

65 Thr Pro Leu Gln Asp Trp Ala His Ala Gly Leu Arg Asp Leu Ala Val

155

150

66 145

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68 gcg gta ga 69 Ala Val Gl	u Pro Val			Met Glu		Ile Ile	
70 72 tgg ggg gc	165 360 acc	מכמ מכפ	tac aga	170	att toa	175	ccc 576
73 Trp Gly Al				-			
74	180		185			190	
76 gtc tcc gc	_			_			
77 Val Ser Al		Gly Arg		Leu Leu	-	Ala Asp	Asn
78 19		+~~ ~~	200	~~~ ~~~	205	+	+ 672
80 ttt gaa gg 81 Phe Glu Gl							
82 210	, <b>01</b> 11 017	215	Dea Dea	niu iio	220	nia iyi	501
84 caa cag ac	a cgg ggc	cta ctt	ggt tgc	atc atc	acc agc	ctc aca	ggc 720
85 Gln Gln Th	r Arg Gly	Leu Leu	Gly Cys	Ile Ile	Thr Ser	Leu Thr	Gly
86 225		230		235			240
88 cgg gac aa							
89 Arg Asp Ly 90	s Asn Gin 245	val Glu	GIY GIU	Val Gin 250	Val Val	Ser Thr	Ala
92 aca caa tc		מכמ פככ	tac atc		ata tat		gtc 816
93 Thr Gln Se							
94	260		265	0-1		270	
96 ttc cat gg	c gcc ggc	tca aag	acc ttg	gcc ggc	ccc aaa	ggc cca	atc 864
97 Phe His Gl							
98 27	~		280		285		
100 acc cag a							
101 Thr Gln M 102 290	et Tyr Tn	r Asn Va. 29		n Asp Lei	<del>-</del>	Trp Gin	ı Ala
102 230 104 ccc cct g	aa aca ca	_	_	a toc aco	300 ago	age tee	gac 960
105 Pro Pro G							
106 305		310		315			320
108 ctc tat t	tg gtc ac	g aga ca	t gcc ga	c gtc att	ccg gtg	cgc cgg	cgg 1008
109 Leu Tyr L	eu Val Th	r Arg Hi	s Ala As	p Val Ile	e Pro Val	Arg Arg	Arg
110	32			330		335	
112 ggc gac a							
113 Gly Asp S 114	er Arg GI 340	y ser Lei	л Leu Se. 34	_	j Pro Val	. Ser Tyr 350	Leu
114 116 aag ggc t		t dac cc:			tea aaa		gtg 1104
117 Lys Gly S							
	55	<u>,,</u>	360	2	365		
120 ggc atc t	tc cgg gc	t gct gtg	g tgc ac	c cgg ggg	g gtt gca	aaa gcg	gtg 1152
121 Gly Ile P	he Arg Al	a Ala Vai	l Cys Th	r Arg Gly	y Val Ala	Lys Ala	Val
122 370		37			380		
124 gac ttc a							
125 Asp Phe I 126 385	ie Pro va		r Met Gl		_	Thr Ser	
128 gct tgg c	at cac co	390 g cag tt/	r aat aa	395 t taa	)		1230
120 get tyg e 129 Ala Trp A							1230
130	40		- 01, 01,	1			
133 <210> SEQ	ID NO: 2						

Input Set : A:\seqlist.txt

Output Set: N:\CRF3\01022002\J017736.raw

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				NCE:												
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140	1				5					10	_				15	
	Leu	Ala	Leu		Thr	Leu	Ser	Pro	_	Tyr	Lys	Val	Leu		Ala	Arg
142	_			20	_		_	_	25		_			30	•	_
143	Leu	He	Trp	Trp	Leu	GIn	Tyr	Leu 40	Ile	Thr	Arg	Val	Glu 45	Ala	His	Leu
145	Gln	Val	Trp	Ile	Pro	Pro	Leu	Asn	Val	Arg	Gly	Gly	Arg	Asp	Ala	Ile
146		50					55					60				
147	Ile	Leu	Leu	Thr	Cys	Ala	Val	His	Pro	Glu	Leu	Ile	Phe	Asp	Ile	Thr
148						70					75					80
	Lys	Leu	Leu	Leu		Ile	Phe	Gly			Met	Val	Leu	Gln		Gly
150			_		85	_				90					95	
	IIe	Thr	Lys		Pro	Tyr	Phe	Val		Ala	Gln	Gly	Leu		Arg	Ala
152	<b>~</b>	36.4.	<b>.</b>	100		_			105	<b>a</b> 1	•	_		110		
	Cys	мет		vai	Arg	гаг	АТА		GIY	GTĀ	His	Tyr		GIN	мет	Ата
154	Dho	Mot	115	T 011	7 l a	7 l a	T 011	120	C1	Шhъ	Птт	37-1	125	7 ~~	1114.0	T 011
156	Pne	130	гуу	ьeu	АІа	Ald	135	THE	GLY	THE	Tyr	140	TAT	ASP	птѕ	ьeu
	Thr		T.e.11	Gln	Acn	Ψrn		ніе	Δla	Glv	T.e.u		λen	T.e.ii	<b>Δ</b> 1 =	Val
	145	110	Deu	OIII	иор	150	nια	1113	nia	GLY	155	nrg	vsb	цец	nia	160
		Val	Glu	Pro	Val		Phe	Ser	Asp	Met	Glu	Val	Lvs	Tle	Tle	
160					165					170	0		_1_		175	
	Trp	Gly	Ala	Asp		Ala	Ala	Cys	Gly		Ile	Ile	Ser	Gly		Pro
162	-	-		180				-	185	-				190		
163	Val	Ser	Ala	Arg	Arg	Gly	Arg	Glu	Ile	Leu	Leu	Gly	Pro	Ala	Asp	Asn
164			195					200					205			
165	Phe	Glu	Gly	Gln	Gly	Trp	Arg	Leu	Leu	Ala	Pro	Ile	Thr	Ala	Tyr	Ser
166		210					215					220				
		Gln	Thr	Arg	Gly		Leu	Gly	Cys	Ile		Thr	Ser	Leu	Thr	Gly
	225				_	230	_		_		235					240
	Arg	Asp	Lys	Asn		Val	Glu	Gly	Glu		Gln	Val	Val	Ser		Ala
170	m1	<b>01</b>	<b>a</b>	D1	245		m)	~		250	<b>a</b> 1	1			255	1
	Thr	GIn	Ser		Leu	Ата	Thr	Cys		Asn	Gly	vaı	Cys	_	Thr	Val
172	Dho	ui o	C1	260	C1	Co.~	T ***	шь×	265	71-	C1	Dro	T	270	Dwo	т1 о
				АІА		ser				АІА	Gly		285		PIO	iie
										λαη	T.Au				Cln	Ala
176	1111	290	nec	- Y -	1111	non	295	изр	GIII	ирь	ьсu	300	GLY	пр	GIII	AIG
	Pro		Glv	Ala	Ara	Ser		Thr	Pro	Cvs	Thr		Glv	Ser	Ser	Asp
	305		1		3	310				J 5	315	J 5	1	501	501	320
		Tyr	Leu	Val	Thr		His	Ala	Asp	Val		Pro	Val	Ara	Ara	Arg
180		<b>4</b> -			325	ر -			- E	330					335	
	Gly	Asp	Ser	Arg		Ser	Leu	Leu	Ser	Pro	Arg	Pro	Val	Ser		Leu
182	-	-		340	-				345		_			350	-	
183	Lys	Gly	Ser	Ser	Gly	Gly	Pro	Leu	Leu	Cys	Pro	Ser	Gly	His	Ala	Val

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			255					260					265				
184	_		355		_	_	_	360	_		_		365		_		
	Gly		Phe	Arg	Ala	Ala		Cys	Thr	Arg	Gly		Ala	Lys	Ala	Val	
186		370					375					380					
187	Asp	Phe	Ile	Pro	Val		Ser	Met	Glu	Thr		Met	Arg	Thr	Ser	Ser	
188	385					390					395					400	
189	Ala	Trp	Arg	His	Pro	Gln	Phe	Gly	Gly								
190					405												
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194	<213	l> Li	ENGTI	H: 10	011												
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200	00 <222> LOCATION: (1)(1005)																
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204	Met	Lys	Lys	Lys	Lys	Leu	Glu	His	His	His	His	His	His	Thr	Ser	Ala	
205	1				5					10					15	÷	
						_				_		-	ggg			_	96
208	Gly	Ile	${ t Thr}$	Lys	Val	Pro	Tyr	Phe	Val	Arg	Ala	Gln	Gly	Leu	Ile	Arg	
209				20					25					30			
													tat				144
212	Ala	Cys	Met	Leu	Val	Arg	Lys	Ala	Ala	Gly	Gly	His	Tyr	Val	Gln	Met	
213			35					40					45				
215	gcc	ttc	atg	aag	cta	gct	gcg	ctg	aca	ggt	acg	tac	gtt	tat	gac	cat	192
216	Ala	Phe	Met	Lys	Leu	Ala	Ala	Leu	Thr	Gly	Thr	Tyr	Val	Tyr	Asp	His	
217		50					55					60					
													cga				240
220	Leu	Thr	Pro	Leu	Gln	Asp	$\mathtt{Trp}$	Ala	His	Ala	Gly	Leu	Arg	Asp	Leu	Ala,	
221	65					70					75					80	
223	gtg	gcg	gta	gag	ccc	gtc	atc	ttc	tct	gac	atg	gag	gtc	aag	atc	atc	288
224	Val	Ala	Val	Glu	Pro	Val	Ile	Phe	Ser	Asp	Met	Glu	Val	Lys	Ile	Ile	
225					85					90					95		
227	acc	tgg	ggg	gcg	gac	acc	gcg	gca	tgc	ggg	gac	atc	att	tca	ggt	ctg	336
	Thr	$\mathtt{Trp}$	Gly	Ala	Asp	Thr	Ala	Ala	Cys	Gly	Asp	Ile	Ile	Ser	Gly	Leu	
229				100					105					110			
												-	gga	_	-		384
	Pro	Val		Ala	Arg	Arg	Gly		Glu	Ile	Leu	Leu	Gly	Pro	Ala	Asp	
233			115					120					125				
													atc				432
	Asn		Glu	Gly	Gln	Gly	_	Arg	Leu	Leu	Aļa	Pro	Ile	Thr	Ala	$\mathtt{Tyr}$	
237		130					135					140					
													acc				480
		Gln	Gln	Thr	Arg		Leu	Leu	Gly	Cys		Ile	Thr	Ser	Leu		
	145					150					155					160	
													gtg				528
	Gly	Arg	Asp	Lys		Gln	Val	Glu	Gly		Val	Gln	Val	Val		Thr	
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247	gct	aca	caa	tct	ttc	ctg	gcg	acc	tgc	gtc	aac	ggc	gtg	tgt	tgg	act	576

Input Set : A:\seqlist.txt

Output Set: N:\CRF3\01022002\J017736.raw

0.40		m1	<b>~</b> 3	<b>a</b>	<b>5</b> 1	<b>-</b>	- 1 -	m\.	_		_	_,	,	_		m1	
	Ala	Tnr	GIn	180	Pne	Leu	Ala	Thr	Cys 185	vaı	Asn	GIĀ	vaı	Cys 190	Trp	Thr	
249	ata	++~	cat		acc	aac	+ < =	224		++~	acc	~~~	000		ggc	cca	624
															Gly		024
253	val	1	195	OT I	1114	O <sub>1</sub>	DCI	200	1111	1100	1114	017	205	Lys	011	110	
	atc	acc		atσ	tac	act	aat		σac	cag	gac	ctc		aac	tgg	caq	672
									-						Trp		
257		210			-1-		215				E	220		1	1		
259	qcq	ccc	cct	qqq	qcq	cqc	tcc	atq	aca	cca	tgc	acc	tgc	qqc	agc	tcg	720
															Ser		
261	225					230					235					240	
263	gac	ctc	tat	ttg	gtc	acg	aga	cat	gcc	gac	gtc	att	ccg	gtg	cgc	cgg	768
264	Asp	Leu	Tyr	Leu	Val	Thr	Arg	His	Ala	Asp	Val	Ile	Pro	Val	Arg	Arg	
265					245					250					255		
															tcc		816
	Arg	Gly	Asp	Ser	Arg	Gly	Ser	Leu	Leu	Ser	Pro	Arg	Pro	Val	Ser	Tyr	
269				260					265					270			
															cac		864
	Leu	Lys	_	Ser	Ser	Gly	Gly		Leu	Leu	Cys	Pro		Gly	His	Ala	
273			275					280					285				
															aaa		912
	vaı	_	IIe	Pne	Arg	Ата		vaı	Cys	Thr	Arg	_	vaı	Ата	Lys	Ala	
277	~+ ~	290	++-	- <del>+</del> -	+	+-	295	+-+		~~~		300	-+-		- <del>-</del> +		060
															act Thr		960
	305	ASP	FIIC	116	PIO	310	Giu	Ser	Met	GIU	315	1111	Met	AIG	1111	320	
		act	taa	cgt	cac		cad	ttc	aat	aat		ааσ	222	ааσ	taa	520	1005
				Arg								_		_	*		1005
285				5	325				1	330		_1_	_1_	-1-			
	ggat	cc	-														1011
			EQ II	ON C	: 4												
				H: 33													
291	<212	2> T	PE:	PRT													
292	<213	3> OI	RGAN	ISM:	HCV												
				NCE:													
295	Met	Lys	Lys	Lys	Lys	Leu	Glu	His	His	His	His	His	His	Thr	Ser	Ala	
296	1				5					10					15		
	Gly	Ile	Thr	_	Val	Pro	Tyr	Phe		Arg	Ala	Gln	Gly	Leu	Ile	Arg	
298				20	_				25	_				30	_		
	Ala	Cys		Leu	Val	Arg	Lys		Ala	Gly	Gly	His	_	Val	Gln	Met	
300			35	_	_			40				_	45	_	_	•	
	Ата		Met	ьys	Leu	Ата		Leu	Thr	GIĀ	Thr		Vai	Tyr	Asp	Hls	
302	T	50	Dmo	т	C1 =	3	55	31.	77.5	71-	C1	60	<b>3</b>	<b>.</b>	T	21-	
303		THE	PTO	ьeu	GIII	70	тгр	Ald	HIS	Ата		Leu	Arg	Asp	Leu		
		λ1-	Wa 1	c1	Dro		Tla	Dha	C.~	λ c.~	75 Met	C1.,	3707	T ***	Ile	80	
305	val	тта	val	GIU	85	vaı	TIG	FILE	SCT	90	met	GIU	val	пåв	95	TTE	
	Ψhr	ሞተካ	Glv	Δla		Пhr	Δla	Δla	Cve		Aen	Tlo	Tle	Ser	Gly	ī.eu	
308				100					105	O-1	p			110	O 1 1	u	
555									100								

Use of n and/or Xaa has been detected in the Sequence Listing. Review the Sequence Listing to insure a corresponding explanation is presented in the <220> to <223> fields of each sequence using n or Xaa.

VERIFICATION SUMMARY

DATE: 01/02/2002

PATENT APPLICATION: US/10/017,736

TIME: 11:32:10

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L:11 M:270 C: Current Application Number differs, Replaced Current Application No

L:11 M:271 C: Current Filing Date differs, Replaced Current Filing Date

L:851 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:19 L:870 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:20